From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING TRANSMITTAL OF COPY OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (CHAPTER I OF THE PATENT COOPERATION TREATY)
(PCT Rule 44bis.1(c))

To:

HØIBERG A/S
St. Kongensgade 59A
DK-1264 Copenhagen K
DANEMARK

Date of mailing *(day/month/year)*	
29 December 2005 (29.12.2005)	
Applicant's or agent's file reference	**IMPORTANT NOTICE**
P779PC00	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/DK2004/000410	11 June 2004 (11.06.2004)	13 June 2003 (13.06.2003)

Applicant

IDH HOLDING ApS et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference P779PC00	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/DK2004/000410	International filing date *(day/month/year)* 11 June 2004 (11.06.2004)	Priority date *(day/month/year)* 13 June 2003 (13.06.2003)]
International Patent Classification (IPC) or national classification and IPC [7] A61K 31/7016, 31/70, A61P 15/02		
Applicant IDH HOLDING ApS		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 11 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 13 December 2005 (13.12.2005)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Simin Baharlou
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Form PCT/IB/373 (January 2004)

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/DK2004/000410	11.06.2004	13.06.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/7016, A61K31/70, A61P15/02

Applicant
IDH HOLDING APS

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 24 and 25 (with respect to industrial applicability)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 24 and 25 (with respect to industrial applicability)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	14, 15, 17, 20, 21, 23
	No:	Claims	1-13, 16, 18, 19, 22, 24-27
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-29
Industrial applicability (IA)	Yes:	Claims	1-23, 26-29
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III.

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

III.1. Article 34(4)(a)(I) PCT

Claims 24 and 25 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

III.2. Article 6 PCT

III.2.1. Present claims 1 and 4 relate to saccharides, defined by reference to a desirable characteristic or property, namely their fermentability by lactic acid bacteria, and their lack of fermentability by *Gardnerella vaginalis*, respectively.

III.2.2. The claims cover all these saccharides, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such saccharides. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

III.2.3. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

III.2.4. Consequently, an International Search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, i.e. those parts wherein the saccharide is selected from saccharose and lactose.

III.2.5. As the ISR for the present application has been limited to subject-matter as defined under item III.2.4, this Written Opinion has been established only for those parts of the subject-matter of the present claims for which an International Search has been performed, namely those parts that have been specified under item III.2.4.

Re Item V.

Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability

V.1. The following documents are referred to:

D1: US-A-3 860 707 (WOOTTON LESLIE WILLIAM) 14 January 1975 (1975-01-14)
D2: US-A-5 314 904 (EGIDIO MARCHI ET AL) 24 May 1994 (1994-05-24)
D3: GB 681 105 A (TAMPAX INC) 15 October 1952 (1952-10-15)
D4: US-B-6 440 9491 (ZENG ZHONGMING) 27 August 2002 (2002-08-27)

V.2. Novelty (Article 33(2) PCT)

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-13, 16, 18, 19, 22 and 24-27 is not new in the sense of Article 33(2) PCT.

V.2.1. The **document D1** (US 3 860 707)

discloses the use of a composition containing about 50% by weight of the disaccharide lactulose for the treatment of vaginitis, characterised - *inter alia* - by the occurrence of vaginal discharge. The treatment as disclosed in D1 resulted in a significant reduction or even suppression of the vaginal discharge, cf. column 4, lines 31-32 and lines 56-57.

The disclosure of document D1 is therefore novelty-destroying for the subject-matter of present claims 1, 3, 5, 7-9, 13, 18, 19, and 24-26.

V.2.2. The **document D2** (US 5 314 904)

discloses the use of a vaginal pharmaceutical composition administrable through the topical route comprising rifaximin, 72% by weight of lactose (disaccharide), and 12% by weight of corn starch (polysaccharide) (Example 10) for the treatment of bacterial vaginosis (BV), including BV caused by *Gardnerella vaginalis* (claims 1-3). The presence of BV was determined - *inter alia* - by a "fishy odor of the vaginal secretion" (column 8, line 5).

The disclosure of document D2 is novelty-destroying for the subject-matter of claims 1-13, 16, 18, 19, 22 and 24-27.

V.2.3. The **document D3** (GB 681 105)
discloses a pharmaceutical composition for vaginal application containing 20% by weight of lactose (Example 1 on page 3).

The disclosure of document D3 is novelty-destroying for the subject-matter of claims 26 and 27.

V.3. Inventive step (Article 33(3) PCT)
The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-29 does not involve an inventive step in the sense of Article 33(3) PCT.

IV.3.1. Problem to be solved
The problem to be solved by the present application is to be seen in the provision of a medicament for the treatment of one or more symptoms caused by bacterial vaginosis.

According to the description, page 5, lines 26-29, the term "symptoms associated with bacterial vaginosis" is to be interpreted as encompassing the symptoms of bacterial vaginosis, "independent of whether the diagnosis of bacterial vaginosis has been established according to the criteria set forth above" (in the description) or not.

IV.3.2. Solution
The solution to the above problem is to use a saccharide, fermentable by lactic acid bacteria, for the preparation of a medicament, the medicament comprising at least 20% by weight of this saccharide.

V.3.3. Prior art
The disclosure of document D4
significantly overlaps with the content of the present application, see item V.3.4.

V.3.4. Difference between present application and document D4
The only relevant difference between the present application and the disclosure of D4, which has been selected as the closest prior art, seems to reside in the amount of saccharide(s) used. In D4, this amount is limited to a range of 2.5 to 17% (w/v) of sucrose and/or maltose, and optionally one or more saccharides selected from the group consisting of glucose, fructose, galactose, mannose, lactose, lactulose, mycose, cellobiose,

melibiose, melitose, malto-oligosaccharide, iso-malto-oligosaccharide and oligo-fructose, dextrin, starch and glycogen can be present.

V.3.4. Analysis of inventive step
Both problem and technical solution appear to be almost identical in the present application and in document D4, the only difference residing in the content of the saccharides in the medicament.

The person skilled in the art, with the knowledge of the disclosure of document D4, aware of any of the disclosures D1 or D3 regarding medicaments having a high content of saccharides, including lactose, for the treatment of symptoms of bacterial vaginosis, would, without the exercise of any inventive skill other than expected from him, consider - in a standard and straightforward optimisation procedure - increasing the content of the oligosaccharides named in document D4, including the lactose concentration, see item V.3.4, in trying to find an alternative or better medicament.

V.3.5. This straightforward variation of the medicament and method for treating bacterial vaginosis in document D4 cannot account for the presence of an inventive step, though.

In view of the successful treatment procedure of document D4, and the limited success of the treatment as used in the present application, see page 13, line 19, it appears that the medicament of the present invention does not provide an unexpected beneficial, superior pharmaceutical effect than the medicament of D4, which could have supported the presence of an inventive step.

V.3.6. In the discussion about the document D4 in the description, the applicant argues that none of the concentrations used in D4 shows a significant decrease in pH, and furthermore, non of the concentrations shows elimination of the odour causing bacteria, the Gram negative bacteria (G-b).

It is evident, however, from Table 4, that the compositions used in D4 indeed result in a decrease of pH and also in a significant decrease of Gram negative bacteria (G - b), see, e.g., the entry for fructose [(G - b) ++++ to ++ within 24 hours and to + within 48 hours.

V.3.7. The subject-matter of present claims 1-29 therefore lacks an inventive step in the sense of Article 33(3) PCT.

V.4. Industrial applicability (Article 33(4) PCT)

For the assessment of the present claims 24 and 25 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.